Sensitivity of Newer-Generation Computed Tomography Scanners for Subarachnoid Hemorrhage: A Bayesian Analysis

Christopher Gee, et al

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1. This is relatively an unimportant paper but does offer a good discussion of the topic. Their study had 134 patients but it was retrospective. Their conclusions were that a negative CT has a sensitivity of 97.8% and that no patient in their study with a negative CT required surgery.

2. Their paper is also one of the first papers that had a good discussion on the strategy of CT/CTA rather than CT/LP.

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Original Contributions

SENSITIVITY OF NEWER-GENERATION COMPUTED TOMOGRAPHY SCANNERS FOR SUBARACHNOID HEMORRHAGE: A BAYESIAN ANALYSIS

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☐ Abstract—Background: Subarachnoid hemorrhage (SAH) is a life-threatening condition considered in patients presenting to the emergency department (ED) with acute and severe-onset headache. Currently, the practice pattern for suspected SAH is to perform a non-contrasted computed tomography (CT) scan of the head, followed by lumbar puncture (LP) if the CT is negative. Newer-generation 16-slice CT scanners have been shown in one study to be very sensitive for SAH. Objective: We sought to validate these findings at our institution by retrospectively analyzing the sensitivity of our 16-slice or better CT scanner and performing a bayesian analysis with the results. Methods: We utilized ED electronic medical records and the Department of Neurosurgery research database to search for patients admitted from the ED with a diagnosis of SAH from January 1, 2005 to December 31, 2008. We found a total of 134 patients admitted with SAH during this time frame. Results: Average age was 53.8 years; 62% were female. Presenting complaint was headache in 57%, paresthesia or weakness in 7%, unresponsive in 10%, confusion or altered mental status in 5%, and "other" in 10%. Sensitivity of 16-slice or better CT scanner in our study was 131/134, or 97.8% (95% confidence interval 93.1–99.4%). No patient with a negative CT had a lesion requiring intervention. Conclusion: Our study confirms the high sensitivity of 16-slice or better CT scanners for SAH. This calls into question the need for LP after negative head CT when 16-slice CT or better is used. © 2012 Elsevier Inc.

☐ Keywords—subarachnoid hemorrhage; CT scan; lumbar puncture; bayesian analysis

INTRODUCTION

It has been estimated that 2% of all emergency department (ED) visits are for a chief complaint of headache (1). Although most of these visits are ultimately primary headaches, an emergency physician is tasked with identifying the life-threatening causes of headaches in these patients. Subarachnoid hemorrhage (SAH) is certainly one of these causes, with a reported mortality of 40% (2). This makes SAH a commonly thought of, but rarely diagnosed, disease. Physicians spend a good deal of time investigating this diagnosis and attempting to minimize the misdiagnosis rate. However, despite the high awareness for SAH, it is still a commonly missed diagnosis (3). Experts believe there are three factors that lead to missed diagnoses: failure to consider SAH in the differential diagnosis, failure to perform computed tomography (CT) scan, and failure to perform and properly analyze the results of lumbar puncture (4–11).

The currently accepted procedure for the work-up of a patient with a possible SAH in the ED is a non-contrast CT scan of the head, followed by a lumbar

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puncture (LP) if the CT is negative for SAH (12). However, there are significant potential risks with performing LP, including its inherently invasive nature, high false-positive rate, difficult interpretation, and complications like persistent cerebral spinal fluid (CSF) leak, epidural hematoma, CSFoma (loculation of CSF near the tap site), epidural abscess, and meningitis. The most common complication of LP is persistent CSF leak, with up to 30–70% of LPs resulting in post-LP headaches (13–15). Use of pencil-point-type spinal needles may reduce these headaches. Additionally, there is patient anxiety and pain associated with the test.

Although the ideal LP provides clear evidence of red blood cells (RBC) that don't clear in successive tubes with spectrographic xanthochromia, this can be difficult to interpret in a traumatic tap with large numbers of RBCs. Furthermore, the xanthochromia can require 12 h or more to develop as RBCs disintegrate in the CSF, leaving bilirubin pigment to color the fluid.

Sensitivity of CT for SAH has been reported to be from 90% to 100% (16–24). However, the studies that report lower sensitivities quite frequently use older-generation CT scanners with fewer slices instead of newer 16- to 64-slice scanners. A recent study by Lourenco et al. used only 16-slice CT scanners and reported the sensitivity of CT for SAH to be 97%, with 60/61 patients diagnosed by CT (19). The final patient was diagnosed by cerebral angiography. We sought to validate these recent results and help determine the sensitivity of newer-generation CT scanners by performing a bayesian analysis using this study by Lourenco et al. as the informed prior (19).

METHODS

The study was performed on patients admitted through the ED. The hospital is an urban referral center with a large catchment area. The annual ED census is > 40,000 patients. We accessed the ED electronic medical records and the Department of Neurosurgery research database to identify all patients admitted from the ED with a diagnosis of SAH from January 1, 2005 to December 31, 2008. Although the CT scanner type from outside hospitals was not known, the CT scanner was upgraded from a 16-slice CT scanner to a 64-slice scanner in early 2005. Unfortunately, during this period, both scanners were used randomly according to CT tech preference and ED work flow. Therefore, it is impossible to identify which scanner was utilized for each patient because this was never documented or recorded.

We evaluated all patients admitted to the hospital with a diagnosis of SAH. The chart review was performed by a single junior physician (post-graduate year 1), with quality assurance (QA) performed on 20% of the charts by a principal investigator who reviewed those selected charts for agreement with initial categorization. No changes from the initial categorization were made on the selected charts. Chart review was performed using standard definitions and a standardized abstraction sheet. We met regularly to answer questions regarding the chart review and to provide feedback as needed. Additional QA was performed by three of the other lead investigators on all charts in which patients had an SAH but negative CT of the head. This QA was to ensure proper categorization of those patients with CT-negative SAH. All of these cases were deemed to be correctly categorized by the initial reviewer. The study protocol was approved by the Institutional Review Board at the hospital.

Statistical Methods

We employed bayesian methods to model remaining uncertainty regarding the location of the parameter of interest (the sensitivity of newer-generation CT for the detection of SAH) in light of prior beliefs and present data. We used the highly flexible family of beta probability distributions for this purpose, which are defined on the interval 0 and 1 (thus making them suitable for the modeling of a proportion) and can be fully described by two parameters, a and b, where $a = $ the number of successes $(s) + 1$ and $b = $ the total number of trials $(n) - s + 1$.

We used the only previous study we could find on the sensitivity of newer-generation CT scanners for SAH as the basis of an empirical prior (19). This smaller study reported the detection of SAH in 60/61 patients evaluated by CT. Thus, we used a beta distribution with $a = 61$ and $b = 2$ to represent prior beliefs regarding this parameter. This prior was combined with present data to arrive at a posterior probability distribution representing a mathematically coherent updated belief regarding the sensitivity of CT for SAH.

To compute and graph probability distributions, we used the freely available R statistical software (R 2.9.2, The R Foundation for Statistical Computing, Vienna, Austria). We report median values and 95% credible intervals (CrI) for all distributions. Credible intervals, unlike traditional confidence intervals, represent where a coherent individual would place 19:1 betting odds on the location of the parameter, given prior beliefs.

RESULTS

There were 134 patients admitted with the diagnosis of SAH during the study period. Presenting chief complaint was headache in 57%, paresthesia or weakness in 7%, unresponsive in 10%, confusion or altered mental status in 5%, and "other" in 10% (Figure 1).

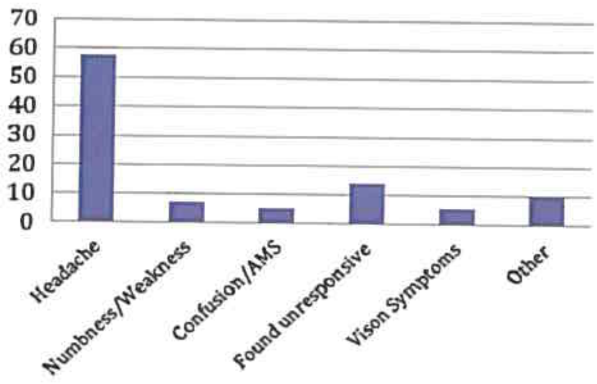

Figure 1. Chief complaints of patients that presented with subarachnoid hemorrhage. Bars represent percent values of total chief complaints. AMS = altered mental status.

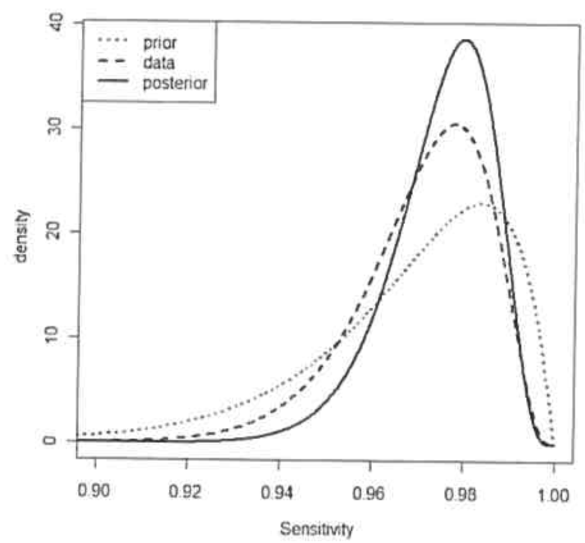

Figure 2. Graphical representation of the probability distributions informing bayesian analysis for the sensitivity of 16-slice (or higher generation) computed tomography in detecting non-traumatic subarachnoid hemorrhage. An empirical prior, based on the results of one similar, smaller study was used to create the prior probability distribution. The likelihood is herein represented as a posterior probability distribution for the present data, under a non-informative or flat prior. Bayes' theorem is used to combine these two functions into a posterior probability distribution representing residual uncertainty regarding the parameter of interest.

Of these 134 patients, 131 had a positive CT by our 16-slice or better CT scanner. Without prior information, this would give a posterior probability distribution with a median sensitivity of 97.3% (95% CrI 91.3–99.6%). Of the 3 patients with a negative CT scan, none required surgical intervention. Two of these patients had no aneurysm on further evaluation and may represent a non-aneurysmal bleed, such as a perimesencephalic bleed, or a traumatic tap. The other one was found to have such a small aneurysm that no intervention was performed on it either.

As mentioned, 2 of the patients with negative CT of the head and positive LP were found to have no aneurysm upon further work-up. One of these had a negative head CT at an outside hospital, but then had an LP with 142 RBCs in tube 1 and 150 RBCs in tube 4. The patient was then transferred to our hospital for evaluation of possible SAH. At our hospital the patient had a negative non-contrast CT of his head, a negative CT angiogram (CTA), and two negative conventional angiograms. Therefore, it would seem that this was either a non-aneurysmal hemorrhage or a traumatic LP.

The other patient with a negative CT of the head, positive LP, and negative work-up for aneurysm had an LP showing RBCs of 3000 in tube 1 and 2200 in a later tube. The patient was then admitted for evaluation of possible SAH. This patient also had a negative CTA and negative conventional angiogram. The patient was then discharged home with Neurosurgery follow-up and no later complications reported. This also could be a non-aneurysmal bleed such as a perimesencephalic bleed or a traumatic LP.

The third patient with a negative CT scan of the head had an LP showing 4200 RBCs in tube 1 and 3500 RBCs in tube 5. The patient then had a CTA showing a 2-mm aneurysm in the anterolateral aspect of the terminal right ICA. The neuroradiologist reviewed the films and determined that the aneurysmal size seen on imaging was so small as to be negligible and would not require any neurosurgical intervention. After consultation with the neurosurgeon, it was decided that the risks of this aneurysm were so small that performing a conventional angiogram would carry more risk than benefit to the patient. The patient's symptoms had resolved at this point and he was discharged home with Neurosurgery follow-up, and no complications were reported 1 year later.

When combined with the informed prior based on Lourenco et al., the median sensitivity of CT for SAH is 97.6 (95% CrI 94.9–99.2) (19). Figure 2 demonstrates graphically the influence of the prior and the likelihood (present data) on the posterior probability distribution. The posterior probability of a sensitivity > 95% was $p = 0.97$. The posterior probability of a sensitivity > 96% was $p = 0.90$.

As mentioned, the three bleeds that were missed required no interventions and were clinically insignificant. This makes the sensitivity of 16-slice or better CT scanners for SAH requiring intervention nearly 100% (median posterior sensitivity 99.6%, 95% CrI 98.1–100%).

DISCUSSION

The current strategy of CT scan followed by LP for the work-up of SAH has been recently questioned. One analysis found LP to be of minimal value in the work-up, whereas others have confirmed that it is necessary (20,21). With the increased sensitivity of newer-generation CT scanners, it has been reported that the negative likelihood ratio of a negative CT scan at < 12 h from onset of symptoms is 0.02 (25). This means that with a pretest probability of 5%, one would have to perform 1000 LPs to pick up one SAH that was missed on CT. Based on estimated complication rates from LP, this would lead to hundreds of post-LP headaches, increasing morbidity and health care costs (26). There may be other less common, but more serious, complications of 1000 LPs, such as cranial neuropathies, prolonged back ache, nerve root injury, meningitis, epidural abscess, and epidural hematoma. Based on the incidence of traumatic, false-positive LPs, the 1000 LPs would lead to 150 unnecessary cerebral angiograms or conventional angiograms, which have a carotid dissection complication rate of 1% (27). With the high rate of complications and false positives from LP, it would be ideal to find a less invasive means to rule out SAH.

A strategy of CT/CTA has also been suggested and found to be 100% sensitive in one small study (28). Another study showed that this strategy can exclude SAH with a > 99% post-test probability (29). However, this leads to increased radiation exposure and risks of dye, and it has not been proven to be 100% sensitive in a large multicenter study. In a recent survey of emergency physicians, it was found that, on average, they wanted a sensitivity of 99% to rule out SAH, and one in five physicians felt that 100% sensitivity was required for a clinical decision rule when evaluating for SAH (30).

No study is 100%, but our results do support the recent study by Lourenco et al. that show the sensitivity of 16-slice CT scanners to be approaching this sensitivity (19). As mentioned in the Results, the three bleeds that were missed required no interventions and were clinically insignificant, making the sensitivity of 16-slice or better CT scanners for SAH requiring intervention nearly 100% (median posterior sensitivity 99.6%, 95% CrI 98.1–100%).

It could be argued that the extremely high sensitivity of CT combined with the potential complication rate of LPs make the LP part of the work-up obsolete and possibly harmful. In our study population, LP added no benefit to any of our patients, as no interventions were performed for the 3 patients with negative CT and positive LP. These patients were, however, exposed to more radiation and procedures that carry an inherent risk of complications and increased medical costs.

Limitations

There are several limitations to this study. First, this was a retrospective study performed at a single center. The results and conclusions would be much stronger had this been performed in a prospective manner at multiple study sites. In addition, despite the desire to delineate the exact number of patients undergoing 16- vs. 64-slice CT scans, this information was not available. The transition between the two scanners was not a clean one, and depending on the day and situation, patients were shifted randomly between the two types of scanners.

A second limitation of the study is that only patients with a diagnosis of SAH were included. Patients who presented to the ED with headache and were discharged with a negative work-up may have represented a population with negative CT and no LP that were not captured in our study data. They may have presented later with SAH to our hospital or another hospital, or they may have died before presenting again. However, no patient was evaluated twice within our dataset. It is the practice in our institution to perform an LP if the CT is negative when working-up a patient for SAH, but there could have been patients who were discharged or left against medical advice before the LP being performed who where missed on CT.

A third limitation is that the time from initial headache onset to performance of the CT scan was not available in the medical record, and was thus not included in our analysis. The timing of the CT scan in relation to the onset of headache may have had an impact on the rate of scans that demonstrated subarachnoid blood.

Finally, although 20% of the charts were selectively reviewed after the initial categorization, this process was not done in a blinded fashion such that a meaningful kappa statistic could be calculated between the two reviewers. This would have lent additional strength to the study's methodology. However, no changes were made to the initial categorization upon review by a principle investigator. In addition, selected cases of SAH that had negative head CT scans were all reviewed by three lead investigators and deemed to be correctly categorized by the first chart reviewer.

CONCLUSION

Our study confirms the high sensitivity of 16-slice or greater non-contrast CT of the head for SAH in our population. It also suggests that the very small false-negative rate of 16-slice or better CT for SAH represents a population with disease that may not be clinically significant. It is unclear if LP adds any additional clinically significant information in the workup of SAH when a 16-slice or better CT scanner is used. Larger, prospective studies are needed to definitively answer this question.

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ARTICLE SUMMARY

1. Why is this topic important?

Headache is a common complaint in the emergency department, and subarachnoid hemorrhage is a key life-threatening diagnosis that must be excluded by emergency physicians. The ever-improving imaging modality of computed tomography (CT) may have reached a point where the performance of potentially dangerous and painful lumbar punctures can be eliminated.

2. What does this study attempt to show?

This study attempts to show the high sensitivity of 16-slice or greater non-contrast CT of the head for subarachnoid hemorrhage (SAH) in our population.

3. What are the key findings?

Sensitivity of 16-slice or better CT scanner in our study was 131/134 or 97.8% (95% confidence interval 93.1–99.4%). No patient with a negative CT had a lesion requiring intervention. It also suggests that the very small false-negative rate of 16-slice CT for SAH represents a population with disease that may not be clinically significant.

4. How is patient care impacted?

It is unclear if lumbar puncture adds any additional clinically significant information in the work-up of SAH when a 16-slice or better CT scanner is used.